

Day : Monday
Date: 2/26/2007

Time: 09:13:52

PALM INTRANET

Inventor Information for 10/642224

Inventor Name	City	State/Country
GOULIAEV, ALEX HAAHT	VEKSO SJ	DENMARK
LARSEN, MOGENS	SMORUM	DENMARK
VARMING, THOMAS	CHARLOTTENLUND	DENMARK
MATHIESEN, CLAUS	VEKSO	DENMARK
JOHANSEN, TINA HOLM	SMORUM	DENMARK
SCHEEL-KRUGER, JORGEN	GLOSTRUP	DENMARK
OLSEN, GUNNAR M.	FREDERIKSBERG	DENMARK
NIELSEN, ELSEBET OSTERGAARD	KOBENHAVEN K	DENMARK

Appln Info

Contents

Petition Info

Atty/Agent Info

Continuity/Reexam

Foreign I

Search Another: Application# Search or Patent# Search
PCT / / Search or PG PUBS # Search
Attorney Docket # Search
Bar Code # Search

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EAST Search History

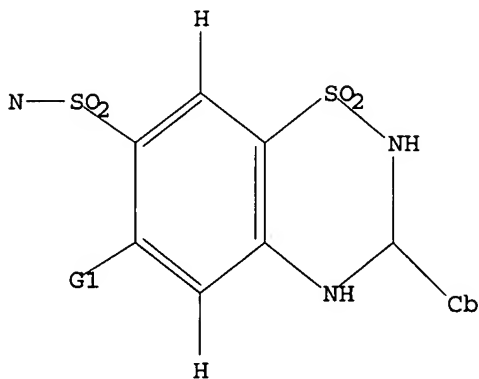
Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	154	544/13.ccls.	US-PGPUB; USPAT	OR	OFF	2007/02/26 08:40
L2	166	514/223.2.ccls.	US-PGPUB; USPAT	OR	OFF	2007/02/26 08:41
L3	285	I1 I2	US-PGPUB; USPAT	OR	OFF	2007/02/26 08:41

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 H, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

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SAMPLE SCREEN SEARCH COMPLETED - 128 TO ITERATE

100.0% PROCESSED 128 ITERATIONS

SEARCH TIME: 00.00.01

5 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 1882 TO 3238

PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

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100.0% PROCESSED 2603 ITERATIONS

SEARCH TIME: 00.00.01

84 ANSWERS

L3 84 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

172.10

172.31

FILE 'CAPLUS' ENTERED AT 08:25:37 ON 26 FEB 2007

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FILE LAST UPDATED: 25 Feb 2007 (20070225/ED)

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L4 19 L3

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L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2006:850385 CAPLUS
 DOCUMENT NUMBER: 145:293109
 TITLE: Preparation of nitric oxide enhancing diuretic compounds, compositions and methods of use
 INVENTOR(S): Garvey, David S.; Letts, L. Gordon; Earl, Richard A.; Ezawa, Maiko; Fang, Xinglin; Geaton, Ricky D.; Khanapure, Subhash P.; Lin, Chia-En; Ranatunge, R.; Stevenson, Cheri A.; Wey, Shioh-Jyi
 PATENT ASSIGNEE(S): Nitromed, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 91pp., which which which which
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006189603	A1	20060824	US 2006-360599	20060224
WO 2006091716	A2	20060831	WO 2006-US6375	20060224

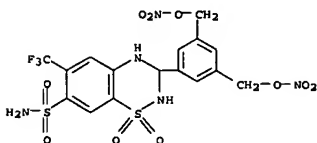
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

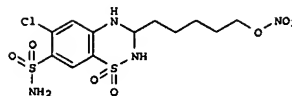
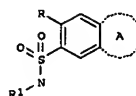
PRIORITY APPLN. INFO.:
 US 2005-655414P P 20050224
 US 2005-656545P P 20050228
 US 2005-685027P P 20050526
 US 2005-692288P P 20050621
 US 2005-749853P P 20051213

OTHER SOURCE(S): MARPAT 145:293109
 GI

L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
 bis((nitrooxymethyl)phenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
 (9CI) (CA INDEX NAME)



L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)



AB The invention describes novel compns. and kits comprising at least one nitric oxide enhancing diuretic compound I [R = Cl or CF₃; R₁ = H, alkyl, cycloalkyl, etc.; Ring A = substituted heterocycle], or pharmaceutically acceptable salts thereof, and, optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. Methods for preparing I are provided. Thus, e.g., II was prepared by cyclocondensation of 6-(nitrooxy)hexenal (preparation given) with 2-amino-6-chloro-1,3-benzenedisulfonamide. Assays for determining diuresis are described (data given). The invention also provides methods for (a) treating conditions resulting from excessive water and/or electrolyte retention; (b) treating cardiovascular diseases; (c) treating renovascular diseases; (d) treating diabetes; (e) treating diseases resulting from oxidative stress; (f) treating endothelial dysfunctions; (g) treating diseases caused by endothelial dysfunctions; (h) treating cirrhosis; (j) treating pre-eclampsia; (k) treating osteoporosis; (l) treating nephropathy; (m) treating peripheral vascular diseases; (n) treating portal hypertension; (o) treating central nervous system disorders; (p) treating metabolic syndrome; (q) treating sexual dysfunctions; and (r) hyperlipidemia. The nitric oxide enhancing diuretic compds. comprise at least one nitric oxide enhancing group linked to the diuretic compound through one or more sites such as carbon, oxygen and/or nitrogen via a bond or moiety that cannot be hydrolyzed.

IT 907624-13-9P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of benzothiadiazine nitric oxide deriva. as diuretics)
 RN 907624-13-9 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-[3,5-

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 1999:549265 CAPLUS
 DOCUMENT NUMBER: 131:184974
 TITLE: Preparation of benzothiadiazines, quinoxalines, and other aryl-fused heterocycles as positive AMPA-receptor modulators for treatment of memory and learning disorders
 INVENTOR(S): Gouliarov, Alex Haahr; Larsen, Mogens; Varming, Mathiesen, Claus; Johansen, Tina Holm; Scheel-Kruger, Jorgen; Olsen, Gunnar M.; Nielsen, Elsebet Ostergaard
 PATENT ASSIGNEE(S): Neurosearch A/S, Den.
 SOURCE: PCT Int. Appl., 168 pp.
 CODEN: PIXX03
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942456	A2	19990826	WO 1999-DK70	19990218
WO 9942456	A3	19991007		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, HD, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

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ZA 9609414 A 19970612 ZA 1996-9414 19961108
 CA 2320354 A1 19990826 CA 1999-2320354 19990218
 AU 9925123 A 19990906 AU 1999-25123 19990218
 AU 751384 B2 20020815
 ZA 9901301 A 19990913 ZA 1999-1301 19990218
 TR 200002427 T2 20010122 TR 2000-200002427 19990218
 EP 1071426 A2 20010131 EP 1999-904730 19990218

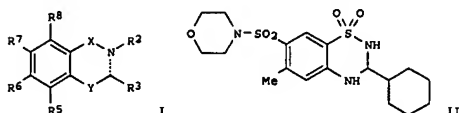
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 JP 20020504481 T 20020212 JP 2000-532408 19990218
 ES 200000468 A 20020415 EE 2000-468 19990218
 RU 2214405 C2 20031020 RU 2000-121882 19990218
 NO 2000004121 A 20001017 NO 2000-4121 20000817
 US 6943159 B1 20050913 US 2000-641814 20000818
 US 2004043987 A1 20040304 US 2003-642224 20020818

PRIORITY APPLN. INFO.:
 DK 1998-226 A 19980218
 WO 1999-DK70 W 19990218
 US 2000-641814 A3 20000818

OTHER SOURCE(S): MARPAT 131:184974
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L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



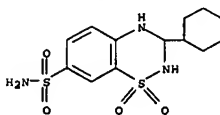
AB Benzothiadiazines, quinoxalines, and other aryl-fused heterocycles (I) [wherein the bond represented by the broken line may be a single, double bond, or absent; and if the bond is absent, then the N is substituted with a H and R2; X = SO₂, CO, or CH₂; Y = -CH(R₄)-, -N(R₄)-, -N(R₄)-CH₂-, or O; R₂, R₄ = H, alkyl, cycloalkyl, aryl, benzyl, substituted carbonyl, or taken together with R₃ = (un)substituted 4-7 membered ring; R₃ = H, (un)substituted cycloalkyl, (un)substituted alkyl, (un)substituted alkoxy, acyl, or taken together with R₂ or R₄ = (un)substituted 4-7 membered ring, etc.; R₅ = H, halogen, alkyl, alkenyl, alkynyl, aryl, or (un)substituted sulfonamido; R₆, R₇, R₈ = H, halogen, (un)substituted alkyl, CN, cyanoalkyl, NO₂, (un)substituted alkoxy, (un)substituted sulfonamido, (un)substituted aryl, etc.] were prepared as pos. AMPA-receptor modulators for treatment of memory and learning disorders. Thus, ClSO₂NCO was added to a cooled solution of m-toluidine and nitroethane or nitromethane followed by addition of AlCl₃ and reaction with H₂SO₄ to form a mixture of 2-amino-6-methylbenzenesulfonamide and 2-amino-4-methylbenzenesulfonamide. The latter isomer was separated by recrystn. and cyclized with cyclohexanecarbonyl chloride in a mixture of TEA, 4-(N,N-dimethylamino)pyridine, and THP to yield dihydro-3-cyclohexyl-6-methyl-1,2,4-benzothiadiazine-1,1-dioxide. The dihydrobenzothiadiazine-1,1-dioxide was chlorosulfonated with chlorosulfonic acid, sulfamoylated with morpholine, and reduced with DIBALH in toluene to give 3-cyclohexyl-6-methyl-7-morpholinisulfonyl-1,2,3,4-tetrahydro-1,2,4-benzothiadiazine-1,1-dioxide (II). Selected compds. of the invention were tested for in vitro inhibition of 3H-AMPA binding and exhibited IC₅₀ values ranging from 3.4 μM to 45 μM. Two compds. were tested and showed significantly increased potentiation of AMPA-induced [3H]GABA release from cultured cortical neurons relative to the potentiation induced by 30 μM cyclothiazide. Expts. were performed in voltage clamp, and all tested compds. reversibly potentiated the current induced by application of 30 μM AMPA. The results of iontophoretic application showed that cyclothiazide did not exhibit any in vivo effects after i.v. administration but that five compds. of the invention enhanced AMPA evoked spike activity in an activity-dependent manner. Passive avoidance expts.

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
were performed to test the pharmacol. effect of compds. on associative memory. Mean entry latency results for each group and the memory enhancing effect of different concns. of one compd. were given.

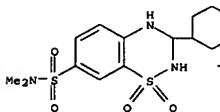
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240139-07-5P 240139-08-6P 240139-09-7P
240139-10-0P 240139-11-1P 240139-12-2P
240139-13-3P 240139-14-4P 240139-59-7P
240139-60-0P 240139-61-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of benzothiadiazines, quinoxalines, and other aryl-fused heterocycles as pos. AMPA-receptor modulators for treatment of memory and learning disorders)

RN 240138-95-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-, 1,1-dioxide (9CI) (CA INDEX NAME)

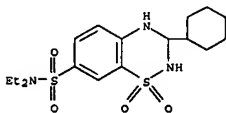


RN 240138-98-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-N,N-dimethyl-, 1,1-dioxide (9CI) (CA INDEX NAME)

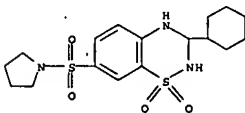


RN 240138-99-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-N,N-diethyl-3,4-dihydro-, 1,1-dioxide (9CI) (CA INDEX NAME)

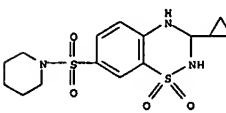
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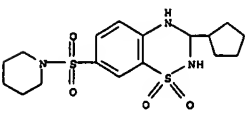
RN 240139-00-8 CAPLUS
CN Pyrrolidine, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 240139-02-0 CAPLUS
CN Piperidine, 1-[(3-cyclopropyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

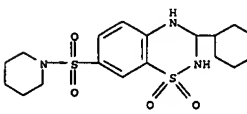


RN 240139-06-4 CAPLUS
CN Piperidine, 1-[(3-cyclopentyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

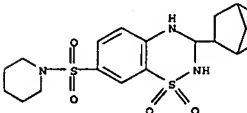


RN 240139-07-5 CAPLUS
CN Piperidine, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

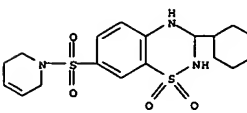
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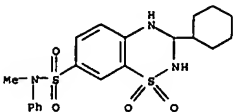
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CN Piperidine, 1-[(3-bicyclo[2.2.1]hept-5-en-2-yl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)



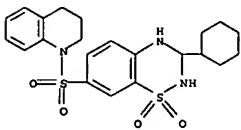
RN 240139-09-7 CAPLUS
CN Pyridine, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]-1,2,3,6-tetrahydro- (9CI) (CA INDEX NAME)



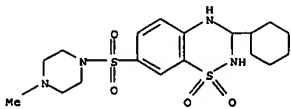
RN 240139-10-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-N-methyl-N-phenyl-, 1,1-dioxide (9CI) (CA INDEX NAME)



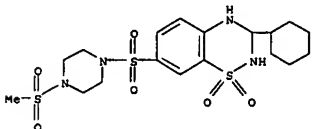
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 RN 240139-11-1 CAPLUS
 CN Quinoline, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



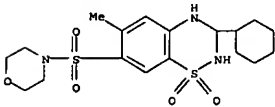
RN 240139-12-2 CAPLUS
 CN Piperazine, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 240139-13-3 CAPLUS
 CN Piperazine, 1-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

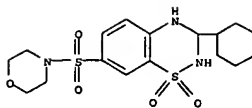


RN 240139-14-4 CAPLUS
 CN Morpholine, 4-[(3-cyclohexyl-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

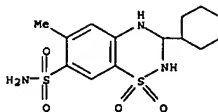


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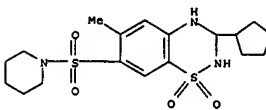
L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 240139-59-7 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-methyl-, 1,1-dioxide (9CI) (CA INDEX NAME)



RN 240139-60-0 CAPLUS
 CN Piperidine, 1-[(3-cyclopentyl-3,4-dihydro-6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 240139-61-1 CAPLUS
 CN Morpholine, 4-[(3-cyclohexyl-3,4-dihydro-6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1984:175285 CAPLUS
 DOCUMENT NUMBER: 100:175285
 TITLE: Substituted 4-phenoxy and 4-phenylthio prolines
 Haugwitz, Rudiger D.; Sprague, Peter M.
 INVENTOR(S): E. R. Squibb and Sons, Inc., USA
 PATENT ASSIGNEE(S): Eur. Pat. Appl., 99 pp.
 SOURCE: CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 95584	A2	19831207	EP 1983-104221	19830429
EP 95584	A3	19840328		
EP 95584	B1	19870107		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8302762	A	19831228	ZA 1983-2762	19830419
CA 1258853	A1	19890829	CA 1983-426141	19830419
AU 8313837	A	19831103	AU 1983-13837	19830421
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JP 04032071	B	19920528		

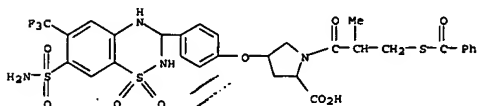
PRIORITY APPLN. INFO.: US 1982-373570 A 19820430

OTHER SOURCE(S): CASREACT 100:175285; MARPAT 100:175285
 01

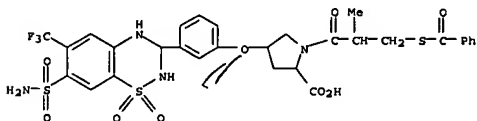
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S; X1, X2 = CHNH, C:N; X3 = CO, SO2; R = H, alkyl, CH2Ph, CHPh2, cation; R1, R2 = H, halo, alkyl, alkoxy, haloalkyl, NO2, SO2NH2, R3 = H, alkyl, cycloalkylalkyl, (un)substituted phenylalkyl, haloalkyl, hydroxyalkyl; R4 = R5SCH2CHR6CO (R5 = H, acyl; R6 = H, alkyl, haloalkyl, Ph, CH2Ph, CH2CH2Ph, cycloalkyl), R8O2CH2CH2NR7CO (R7 = alkyl, cycloalkyl; R8 = same as R), R9O2CHCHR10NHCHR11CO (R9 = same as R; R10 = H, (CH2)mC6H4R12 (R12 = H, alkyl, alkoxy, halo, OH; m = 0-4), (un)substituted alkyl; R11 = H, (CH2)mR12, (un)substituted alkyl, R13P(O) (OR14)CH2CO [R13 = alkyl, (CH2)nR15 (R15 = C6H4R12, thienyl, furyl, pyridyl, cycloalkyl; n = 0-7); R14 = H, alkyl, CH2Ph, CHPh2, ion, CHR17O2CR16 (R16 = H, alkyl, alkoxy, cycloalkyl, Ph, CH2Ph, CH2CH2Ph; R17 = H, alkyl, cycloalkyl, Ph)] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, L-4-hydroxyproline was acylated with D-BzSCH2CHMeCOCl to give BzSCH2CHMeCO-Hyp-OH, which was esterified with MeOH/p-MeC6H4SO3H to give the Me ester, which was treated with m-HOC6H4CH(OMe)2 in the presence of Ph3P to give hydroxyproline II. The cyclocondensation of II with benzamide III gave quinoxaline IV (R18 = Bz,

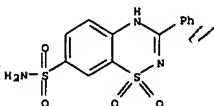
L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
 R19 = Me), which was aspond. to give IV (R18 = R19 = H).
 IT 89813-52-5P 89813-53-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 89813-52-5 CAPLUS
 CN L-Proline, 4-[4-[7-(aminosulfonyl)-3,4-dihydro-1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2a,4a)- (9CI) (CA INDEX NAME)



RN 89813-53-6 CAPLUS
 CN L-Proline, 4-[3-[7-(aminosulfonyl)-3,4-dihydro-1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2a,4a)- (9CI) (CA INDEX NAME)



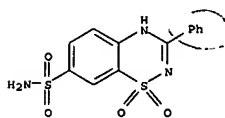
L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1968:496681 CAPLUS
 DOCUMENT NUMBER: 69:96681
 TITLE: Reactions with N-sulfinyl compounds. X. Benzothiadiazine derivatives from N-sulfinylsulfonamides and N-arylamidines
 AUTHOR(S): Kresze, Guenter; Seyfried, Christoph; Trede, Achim
 CORPORATE SOURCE: Tech. Hochsch. Muenchen, Munich, Fed. Rep. Ger.
 SOURCE: Justus Liebig's Annalen der Chemie (1968), 715, 223-37
 CODEN: JLABCF; ISSN: 0075-4617
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 OTHER SOURCE(S): CASREACT 69:96681
 GI For diagram(s), see printed CA issue.
 AB Reaction of 4-RC6H4N:CR1NH2 with R2SO2N:SO (R = H, Cl, Br or SO2NH2, R1 = Ph or 4-ClC6H4, R2 = Me, Ph, or 4-MeC6H4) gave the corresponding I.
 IT 20043-38-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 20043-38-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-phenyl-, 1,1-dioxide (8CI, 9CI)
 (CA INDEX NAME)



L4 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1973:72227 CAPLUS
 DOCUMENT NUMBER: 78:72227
 TITLE: 2H-1,2,4-Benzothiadiazine 1,1-dioxide derivatives
 INVENTOR(S): Kresze, Guenter; Trede, Achim; Seyfried, Christoph
 PATENT ASSIGNEE(S): Schering A.-G.
 SOURCE: Ger., 5 pp.
 CODEN: GWXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1470316	A	19690424	DE 1964-SC35190	19640521
DE 1470316	C3	19730628		
PRIORITY APPLN. INFO.:			DE 1964-SC35190	19640521

GI For diagram(s), see printed CA issue.
 AB R1SO2N:SO reacted with 4-R2C6H4N:CRNH2 in CHCl3 to give the 1-(sulfonylimino)-1,2,4-benzothiadiazines I. Thus, p-MeC6H4SO2N:SO was treated with PhC(:NPh)NH2 to give I (R = Ph, R1 = C6H4Me-p, R2 = H). Similarly, 9 more I (R = Ph, C6H4Cl-p, C6H4Me-p, OMe, Me; R1 = C6H4Me-p, Ph, Me; R2 = Cl, Br, HANSO2) were prepared I were also oxidized to the S-oxides and S,S-dioxides.
 IT 20043-38-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 20043-38-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-phenyl-, 1,1-dioxide (8CI, 9CI)
 (CA INDEX NAME)

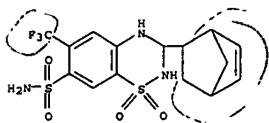


L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1967:10970 CAPLUS
 DOCUMENT NUMBER: 66:10970
 TITLE: 7-Sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide derivatives
 INVENTOR(S): Mueller, Erich; Haasacher, Klaus
 PATENT ASSIGNEE(S): Boehringer Ingelheim G.m.b.H.
 SOURCE: U.S., 6 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3275625		19660927	US	19610123

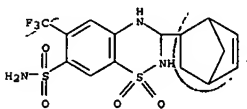
GI For diagram(s), see printed CA issue.
 AB Novel derivs. of 7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, which are substituted in the 3-position by an alicyclic bicyclic radical, can be prepared by the following process. A mixture of 8.5 g. 6-chloro-4-aminobenzene-1,3-disulfonamide, 4 g. 2,5-endomethylene-Δ3-tetrahydrobenzaldehyde, and 25 cc. diethylene glycol dimethyl ether was heated 2 hrs. at 100° and the mixture allowed to stand 14 hrs. at room temperature to give 7.5 g.
 3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 229-30°. Similarly were prepared the following compds.:
 3-(bicyclo[2.2.1]hept-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 263-6°; 3-(2,3-dibromobicyclo[2.2.1]hept-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 199-201°C. (decomposition);
 3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-trifluoromethyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 119°; 3-(bicyclo[2.2.1]hept-2-en-6-yl)-5-methyl-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 190-1°; 3-(bicyclo[2.2.1]hept-2-en-6-yl)-5,6-dichloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 184°; 2-methyl-3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-methylsulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 232-5°; 3-(bicyclo[2.2.2]oct-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 276-7° (decomposition);
 3-(5-methylbicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 197-9°;
 3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 226-30°. Coated pills, suppositories, gelatin capsules, and liquid-containing ampuls are made from the various diuretic compds.
 IT 859-24-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 859-24-5 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

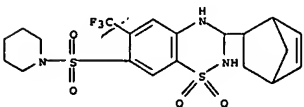


L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

reduced with H and Raney Ni to yield
 J- (bicyclo[2.2.1]hept-6-yl)-6-chloro-
 7- (N-methylsulfonamido)-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide,
 m. 146-8°.
 IT 859-24-8P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide
 4233-37-8P, Piperidine, 1-[[3,4-dihydro-3-(5-norbornen-2-yl)-6-
 (trifluoromethyl)-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]-, S,S-dioxide
 RL: PREP (Preparation)
 (preparation of)
 RN 859-24-5 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
 3,4-dihydro-3-(5-norbornen-2-yl)-
 6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 4233-37-8 CAPLUS
 CN Piperidine, 1-[[3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-2H-
 1,2,4-benzothiadiazin-7-yl]sulfonyl]-, S,S-dioxide (7CI, 8CI) (CA INDEX
 NAME)



L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1965:498466 CAPLUS
 DOCUMENT NUMBER: 63:98466
 ORIGINAL REFERENCE NO.: 63:18126e-h,18127a
 TITLE: 7-Sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine
 1,1-dioxides
 INVENTOR(S): Thomas, Karl
 PATENT ASSIGNEE(S): G.m.b.H.
 SOURCE: 12 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 296964		19650525	NL	
PRIORITY APPLN. INFO.:			DE	19620824

GI For diagram(s), see printed CA Issue.

AB The title compds. (I), useful as diuretics, are prepared Thus, to a
 solution
 of 16.28 g. 6-chloro-4-aminobenzene-1,3-disulfonyl chloride (II) in 50
 ml.
 dry tetrahydrofuran (THF) is added dropwise at 20° under cooling 25
 ml. of a solution containing 12.28 g. MeNH₂ in 100 ml. THF. The mixture
 is diluted
 with 50 ml. acetone, filtered, and evaporated in vacuo at 20°. The
 oily residue is recrystd. twice from 260 ml. 1:1 MeOH-H₂O at -10°
 to yield 3-methylsulfonamido-4-amino-6-chlorobenzene-sulfonyl chloride
 (III), m. 146-8°. Similarly prepared are the following IV (R₄, R₅,
 R₆, and m.p. given): Cl, H, H, 186-7° (V) (78.7% yield); CF₃, H, H,
 161-3° (VI); Cl, H, benzyl, 135-8° (C₆H₅CH₂)₂ (VII) (62%
 yield). To a solution of 1.6 g. III and 15 mg. p-toluenesulfonic acid in
 dioxane is added at 70° 0.61 g. 2,5-endomethylene-1,2,5,6-
 tetrahydrobenzaldehyde (VIII); the mixture is held 20 min. at 70° and
 worked up to yield 2-methyl-3-(bicyclo [2.2.1]
 hept-2-en-6-yl)-6-chloro-7-
 chlorosulfonyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (IX),
 decomposed at 154-9° (MeOH-H₂O). Similarly, V, VI, and VII are
 converted with VIII into the corresponding 3-(bicyclo[2.2.1]hept-
 2-en-6-yl)-7-chlorosulfonyl-3,4-dihydro-1,2,4-benzothiadiazine
 1,1-dioxides (R₄, R₅, R₆, and m.p. given): Cl, H, H, 186-7°
 (MeOH-H₂O) (X); CF₃, H, H, -(XI); Cl, H, benzyl, 188-9° (decomposition)
 (XII). A solution of 1 g. IX in 25 ml. THF is treated 15 min. with
 gaseous
 NH₃ to yield 2-methyl-3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-
 sulfonamido-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m.
 257-8° (EtOH-H₂O). Similarly prepared are the 3-(bicyclo[2.2.1]hept-
 2-en-6-yl)-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I) (R₁: R₂:
 R₃: R₅: H) (R₄, R₆, R₇, R₈, and m.p. given): Cl, Me, H, Me,
 231-3° (MeOH-H₂O); Cl, Me, H, H (XIII), 212-14° (MeOH-H₂O);
 Cl, H, H, H, 226-8° (MeOH-H₂O); CF₃, R₆R₇: piperidino, H,
 133-40° (decomposition); CF₃, H, H, H, 165-8°; Cl, H, H, H,
 benzyl, 222-4° (decomposition). A solution of 0.808 g. XIII in dioxane
 is

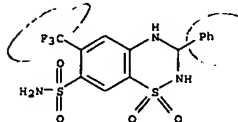
L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1965:51748 CAPLUS
 DOCUMENT NUMBER: 62:51748
 ORIGINAL REFERENCE NO.: 62:9157e-g
 TITLE: 1,2,4-Benzothiadiazine derivatives
 INVENTOR(S): Novello, Frederick C.
 PATENT ASSIGNEE(S): Merck & Co., Inc.
 SOURCE: 2 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3160629		19641208	US 1961-101331	19610407
PRIORITY APPLN. INFO.:			US	19610407

GI For diagram(s), see printed CA Issue.

AB A process leading to the title compds. is described. Thus, 3.75 g. KMnO₄
 is added with stirring over 10 min. to a solution of 8.9 g.
 6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide in
 150
 ml. H₂O and 10 ml. 20% NaOH. The solution is stirred at room
 temperature 15 min.
 and warmed on a steam bath 5 min., EtOH added to destroy excess KMnO₄,
 and
 the solution filtered and acidified to give 6-chloro-7-sulfamoyl-1,2,4-
 benzothiadiazine 1,1-dioxide (I), m. 337°. Similarly prepared is
 6-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 345°.
 IT 1170-25-8P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
 RL: PREP (Preparation)
 (preparation of)
 RN 1170-25-8 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-
 (trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1965:51747 CAPLUS
DOCUMENT NUMBER: 62:51747
ORIGINAL REFERENCE NO.: 62:9157c-e
TITLE: Benzothiadiazine dioxides
INVENTOR(S): Cheney, Lee C.; Holdrege, Charles T.
PATENT ASSIGNEE(S): Bristol Laboratories International, S. A.
SOURCE: 18 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1368708		19640807	FR 1959-806279	19590929
US 3230218		19660118	US 1959-795595	19590226

PRIORITY APPLN. INFO.: US 19580930

OTHER SOURCE(S): MARPAT 62:51747

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) are used for the treatment of edemas associated with

cardiac congestion, cirrhosis of the liver and kidney, and other diseases characterized by excessive accumulation of water. These compds. are obtained by the condensation of an aldehyde with a suitable aniline derivative

Thus, to a solution of 0.09 mole 2-tri-fluoromethyl-4-amino-5-sulfamoylbenzenesulfonyl chloride in 125 cc. dioxane was added 15 cc. 40% CH₂O, the solution added to 125 cc. concentrated NH₄OH, NH₄OH distilled after 1.5

hrs., and the residue refluxed 2.5 hrs. to give I (R = R₁ = H), m. 260-4°. The following I were similarly prepared (R, R₁, and m.p. given): H, Me, 216-21°; H, Et, 256-8° (decomposition) and 262-3° (decomposition) (2 forms); H, Me, 247-50° (decomposition); H, PhCH₂, 221-3°; H, 2-pyridyl, 310-11°; H, Cl₃C, 283-5° (decomposition); H, Ph, 219-21°. By using cyclohexanone ethylene acetal, 7-sulfamoyl-6-trifluoromethylspiro

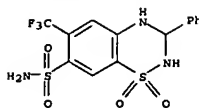
[2H-1,2,4-benzothiadiazine-3,1'-cyclohexane] 1,1-dioxide, m. 260-2°, was obtained.

IT 1170-25-8P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
RL: PREP (Preparation)
(preparation of)

RN 1170-25-8 CAPLUS

CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1963:462475 CAPLUS
DOCUMENT NUMBER: 59:62475
ORIGINAL REFERENCE NO.: 59:11536h,11537a-b
TITLE: Dihydrobenzothiadiazine dioxides
PATENT ASSIGNEE(S): Eli Lilly & Co.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 915216		19630109	GB	
			US	19601031

PRIORITY APPLN. INFO.:

GI For diagram(s), see printed CA Issue.

AB The preparation of

3-(bicyclo[2.2.1]hept-2-en-5-yl)-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I) is described. These compds. are used as diuretic agents. 5-Chloro-2,4-disulfamoylaniline (28.5 g.) was suspended in 195 ml. 95% aqueous EtOH and 150 ml. 6N aqueous HCl, and 12.2 g.

bicyclo[2.2.1]hept-2-en-5-ylcarboxaldehyde added, and the reaction stirred to effect solution of the aldehyde. The mixture was kept at room temperature 12 hrs. and the precipitate of I (R = Cl) filtered off and washed to remove HCl, m.

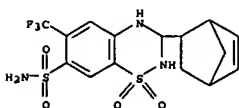
220-1° (EtOAc). Similarly prepared was I (R = CP₃), m. 221°. These compds. were also prepared by cyclizing bicyclo[2.2.1]hept-2-en-5-ylcarboxaldehyde with 1,3-disulfamoyl-4-fluoro-6-chloro(or 6-trifluoromethyl)benzene in the presence of NH₃ or by acylating 1,3-disulfamoyl-4-amino-6-chloro- (or trifluoromethyl)benzene with an anhydride or acid halide of bicyclo[2.2.1]hept-2-enyl-5-carboxylic acid, cyclizing the acylated product produced with an alkali, and then reducing the benzothiadiazine cyclization product to form a dihydrobenzothiadiazine

IT 859-24-5P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide
RL: PREP (Preparation)
(preparation of)

RN 859-24-5 CAPLUS

CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide,

3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

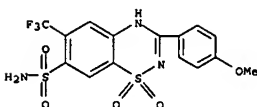


L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

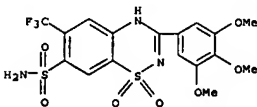
L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN
 ACCESSION NUMBER: 1963:53284 CAPLUS
 DOCUMENT NUMBER: 58:53284
 ORIGINAL REFERENCE NO.: 58:9078c-h
 TITLE: Synthesis of 1,2,4-benzothiadiazine 1,1-dioxide derivatives
 AUTHOR(S): Klose, Josef
 CORPORATE SOURCE: Privatlab., Berlin
 SOURCE: Journal fuer Praktische Chemie (Leipzig) (1962), 18, 313-20
 CODEN: JPCEAO; ISSN: 0021-8383
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 58:53284
 GI For diagram(s), see printed CA issue.
 AB The acylation of 5-trifluoromethyl-aniline-2,4-disulfonamides with carboxylic acids in the presence of POCl₃ and subsequent cyclization of the resulting acylanilide analogs with concentrated H₂SO₄ yielded a series of
 CC. 3-substituted 6-trifluoro-7-aminosulfonyl-1,2,4-benzothiadiazine 1,1-dioxides. 5,2,4-CP₃(H₂NO₂S)C₆H₂NNH₂ (I) (6.4 g.), 2 cc. AcOH, and 6
 POCl₃ heated 10-15 min. with stirring at 60-70° and then to 90-110°, cooled, diluted with 50 cc. H₂O, boiled, cooled, and filtered yielded 6.7 g. N-Ac derivative (II) of I. leaflets, m. 292-4° (80% iso-PrOH) with browning from 250°. I (6.4 g.) in 30 cc. MePh and 2 cc. AcOH refluxed, treated during 15 min. dropwise with 6 cc.
 POCl₃, refluxed 1 hr., cooled, and filtered, and the residue treated with 30 cc. H₂O, heated on the water bath, and worked up in the usual manner yielded 6.8 g. II. Similarly were prepared the following III (R and m.p. given): EtCO, 312-14° (80% iso-PrOH); PrCO, 295-7° (needles); iso-PrCO, 282-4° (60% iso-PrOH); iso-BuCO, 208-10° (gray crystal powder); C₇H₁₅CO, 158-60° ClCH₂CO, 298-300° (with browning from 250°); Cl₂CHCO, 208-10° [resolidified at 220° and remelted at 234° (decomposition)]; CCl₃CO, 228-30° [resolidified at 234° and remelted at 293-5° (decomposition)]; CH₂BrCO, 228-30° (resolidified at 250°); CHBr₂CO, 220-2° (with browning at 210° (decomposition)); MeCHBrCO, 304-6° with sintering an turning brown-yellow from 250°; Me₂CHCHBr, 128-30° (needles); Bz, 250-2° (resolidified at 270° and decompose at 328-30°); p-MeOC₆H₄CO, m. 246-8° (resolidified at 260° and decomposed up to 290°); 3,4,5-(MeO)₃C₆H₂CO, 312-14°; p-MeC₆H₄CO, 165-7° with browning from 250° (needles); PhCH₂CO, 124-6° (80% iso-PrOH); Ph₂CHCO, 228-30° (needles); EtPhCHCO, 162-4° (crystal powder); picolinoyl, 158-60° (crystal powder); nicotinoyl, 226-8° (needles); isonicotinoyl, 233-5° (needles). II (6 g.) added in portions with stirring to 20-30 cc. concentrated H₂SO₄, heated 2-3 hrs. at 60-70°, kept overnight, added slowly with stirring into 50 cc. H₂O and filtered after 2 hrs. gave 5.2 g. (crude) 3-methyl-6-trifluoromethyl-7-aminosulfonyl-1,2,4-benzothiadiazine 1,1-dioxide (IIa), m. 334-6° (iso-PrOH). IIIa (1 g.) in 40 cc. Ac₂O refluxed 5 hrs., filtered hot, and cooled gave 1.1 g. N-Ac derivative (IV) of IIIa, m. 298-300° (80% iso-PrOH) (decomposition). Similarly were prepared the

L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

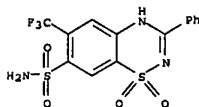
RN 1550-90-9 CAPLUS
 CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-methoxyphenyl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



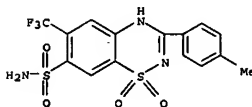
RN 1691-04-9 CAPLUS
 CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-(trifluoromethyl)-3-(3,4,5-trimethoxyphenyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
 following IVa (R and m.p. given): Et (7), 346-8° (decompn.); Pr, 318-20°; iso-Pr, 296-8°; iso-Bu, 235-7°; C₇H₁₅, 203-5°; ClCH₂, 312-14°; Cl₂CH, 306-8°; CCl₃, 293-5°; BrCH₂, 292-4°; Br₂CH, 258-60°; MeCHBr, 306-8° (decompn.); Me₂CHCHBr, 160-2°; Ph, 330-2°; p-MeOC₆H₄, 290-2°; 3,4,5-(MeO)₃C₆H₂, 228-30° (iso-PrOH); p-MeC₆H₄, 280-2°; PhCH₂, 164-6° (80% iso-PrOH); Ph₂CH, 258-60° (iso-PrOH); EtPhCH, 237-9°; 2-pyridyl, 302-4°; 3-pyridyl, 334-6°; 4-pyridyl, 316-18°. IV (1 g.) refluxed 20 min. in 200 cc. H₂O, filtered hot, and cooled gave 0.6 g. IIIa, needles, m. 332-4° (80% iso-PrOH). V with Ac₂O gave in the usual manner the Ac deriv., m. 296-8°, which was hydrolyzed with H₂O to V, needles, m. 346-8°. IIIa (1 g.) and 30 cc. (EtCO)₂O refluxed 6 hrs. yielded 0.9 g. EtCO deriv. (VI) of IIIa, m. 284-6° (decompn.) (80% iso-PrOH); V with (EtCO)₂O gave similarly the EtCO deriv. (VII) of IIIa, m. 280-2° (60% iso-PrOH). VI and VII refluxed with dil. H₂SO₄ yielded IIIa and V, resp.
 IT 746-82-7P, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 859-25-6P, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-p-tolyl-6-(trifluoromethyl)-, 1,1-dioxide 1550-90-9P, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-methoxyphenyl)-6-(trifluoromethyl)-, 1,1-dioxide 1691-04-9P, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-(trifluoromethyl)-3-(3,4,5-trimethoxyphenyl)-, 1,1-dioxide
 RL: PREP (Preparation)
 (preparation of)
 RN 746-82-7 CAPLUS
 CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 859-25-6 CAPLUS
 CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-p-tolyl-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 1963:33410 CAPLUS
 DOCUMENT NUMBER: 58:33410
 ORIGINAL REFERENCE NO.: 58:5689c-h, 5690a
 TITLE: A simple synthesis of dihydrobenzothiadiazine dioxide derivatives

AUTHOR(S): Klose, Josef; Voigt, Hans
 CORPORATE SOURCE: Privates Forschungslabor, Berlin-Zehlendorf
 SOURCE: Journal fuer Praktische Chemie (Leipzig) (1962), 16, 264-76
 CODEN: JPCEAO; ISSN: 0021-8383

DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 58:33410
 AB 6-Chloro- (I) and 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide (II) deriva., substituted at C-3 with R which

was H, alkyl, aryl, or aralkyl, were synthesized by heating 2,4-disulfamoyl-5-chloroaniline (III) or the 5-trifluoromethyl analog (IV), resp., with RCHO (V) in aqueous HCl (EtOH added when III or IV were insol. in water). Nonaq. media were not necessary for the reaction. V which either reacted or did not react with III and IV were tabulated.

Two mechanisms were discussed for the condensation reaction in aqueous media and one in nonaq. media. III (5.7 g.) was suspended in 150 ml. H₂O, 0.02 mole

V and 3 ml. concentrated HCl added, and if H₂O-soluble addnl. 50 ml. H₂O added,

otherwise 50 ml. EtOH added, refluxed 40-60 min., and crystalline I filtered

off hot. II were similarly prepared from IV. Acetals of halogenated V also

condensed with III and IV to yield I and II, resp. Thus, 30 g. III was suspended in 80 ml. H₂O and 50 ml. concentrated HCl, a solution of 18 ml. of the

acetal of BrCH₂CHO in 110 ml. EtOH added, the mixture refluxed 4 hrs., cooled, and the product filtered off and washed with H₂O to yield 38 g. I (R = BrCH₂) (VII), m. 224-6°. Similarly the acetals of ClCH₂CHO and ClCH₂CHO yielded the corresponding I and II. I and II where R =

5-nitro-2-furyl were preferably prepared from 5-nitrofurural diacetate. The following I and II were prepared by the above routes (R and m.p. of I and II given): H, --, 261-3°; Me, 254-6°, 246-8°; Et, 266-8°, 262-4°; Pr, 255-7°, 228-30°; iso-Pr, 290-2°, 248-50°; Bu, 190-2°, 210-12°; iso-Bu, 244-6°, --; CH₂Cl, 334-6°, 237-9°; CHCl₂, 242-4°, 246-6°; CCl₃, 300-2°, --; CH₂Br, 224-6°, 206-8°; CH₂I (VII), 198-200°, 194-6°;

PhCH₂, 246-8°, 220-2°; PhCHMe, 220-4° (when recrystd. from EtOH yielded a soluble form, m. 226-8° and a slightly soluble form, m. 238-48°), 235-7°; PhCH₂CH, 248-50°, 171-3°;

4-pyridyl, 326-8°, --; 2-furyl, 212-14°, 252-4°; 5-nitro-2-furyl, 220-2°, 212-14°; p-ClC₆H₄, 236-8°, 224-6°; p-ONC₆H₄, 242-4°, 235-7°; p-ClC₆H₄CH₂, 238-40°, 246-42°; p-MeOC₆H₄CH₂, 224-6°, 244-6°;

245-7°; p-MeC₆H₄CH₂, 230-2°, --; o-FC₆H₄, 245-7°, 243-5°; m-FC₆H₄, 223-5°, 248-50°; antipyril, 244-6°, oil. VI (20 g.) and 16 g. KI in 200 ml. anhydrous Me₂CO

refluxed 5 hrs., half the solvent evaporated, and H₂O added; 22 g. VII separated

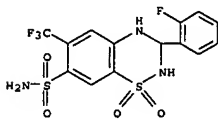
separated

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
 When, however, the reaction was carried out in H₂O or EtOH only decompn. products were obtained. A suspension of 60 g. III, 2.6 l. H₂O, 20 ml. concd. HCl, and 18 ml. 37% aq. HCHO (VIII) was stirred and refluxed 20-30 min. when all dissolved, the mixt. was refluxed 30 min., C added, and the mixt. filtered hot. From the filtrate sepd. on cooling 53 g. cryst. I (R = H) (IX), m. 270-2° (H₂O). IX in hot 0.1N NaOH hydrolyzed to III. Excess VIII in the above reaction caused polymer formation. Thus, when a suspension of 5.7 g. III in 50 ml. H₂O contg. 4 ml. 37% aq. VIII, 2 ml. concd. HCl, and 100 ml. EtOH was refluxed 1 hr., cooled, and 50 ml. H₂O added 6 g. colorless resin (X), m. 265-70°. sepd., sol. in alcohols and other org. solvents. Polymer formation was avoided by carrying out the reaction in aq. NH₃. Thus, a mixt. of 6.8 g. III, 40 ml. concd. aq. NH₃, and 0.7-1 g. VIII (as the 37% aq. soln.) (or a large excess of VIII may also be employed) stirred and refluxed 20-30 min., decolorized with

C. and filtered hot gave 4.5 g. IX, m. 270-2°. IX in 95% yield was also obtained after 1 hr. reflux of 57 g. III, 2.5 l. H₂O, 20 ml. 25% NH₃, and 30 ml. 37% aq. VIII. Mixed m.p.s. of X with III or IX showed no depression, indicating that the wide range of m.p.s. of IX reported (from III and gaseous HCl in nonaq. media) (Freeman and Wagner, CA 46, 1559i) was due to the presence of impurities in IX. The diuretic effects of I and II were tabulated and discussed.

IT 748-17-4P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(o-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide 748-18-5P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(m-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide 748-19-6P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-chlorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide 3872-12-6P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(p-nitrophenyl)-6-(trifluoromethyl)-, 1,1-dioxide

RL: PREP (Preparation of)
 RN 748-17-4 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(o-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (8CI) (CA INDEX NAME)



RN 748-18-5 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(m-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:423273 CAPLUS
 DOCUMENT NUMBER: 57:23273
 ORIGINAL REFERENCE NO.: 57:46859-4, 4686a-b
 TITLE: 7-Sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides
 INVENTOR(S): Mueller, Erich; Messpacher, Klaus
 PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H.
 SOURCE: 4 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

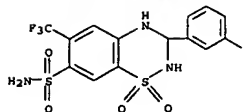
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1125938		19620322	DE 1960-T17869	19600212
GB 906850			GB	
PRIORITY APPLN. INFO.:			DE	19600212

GI For diagram(s), see printed CA issue.
 AB The title compds. substituted in the 3 position with a bicyclic group were prepared by reaction of a 2,4-disulfamoylaniline with a bicyclic aldehyde or a functional derivative thereof. Thus, 8.5 g. 6,4,1,3-C1(H2N)C6H2(SO2NH2)2 and 4.0 g. 2,5-endomethylene-1,2,5,6-tetrahydrobenzaldehyde in 25 cc. bis(2-methoxyethyl)ether was heated 2 hrs. at 100°, the solution left at room temperature 14 hrs., 50 cc. CHCl₃ added, the precipitate filtered off, and dried to give 7.5 g. 3-(6-bicyclo[2.2.1]-2-heptenyl)-6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 129-30° (aqueous MeOH). I (6.0 g.) was hydrogenated in dioxane in the presence of Raney

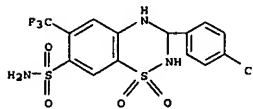
NI to give 3-(6-bicyclo[2.2.1]heptyl)-6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 263-6°. Treatment of 4.0 g. I with 1.6 g. Br in AcOH gave 3.0 g. 3-(6-(2,3-dibromobicyclo[2.2.1]heptyl)-6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 199-201°. II prepared were (R, R1, R2, R3, R4, and m.p. given): H, 6-bicyclo[2.2.1]-2-heptenyl, H, CF₃, H, 119° (AcOH-ligroline); H, 6-bicyclo[2.2.1]-2-heptenyl, Me, Cl, H, 190-1°; H, 6-bicyclo[2.2.1]-2-heptenyl, Cl, Cl, H, 184° (MeOH-H₂O); Me, 6-bicyclo[2.2.1]-2-heptenyl, H, Cl, Me, 232-5°; H, 6-bicyclo[2.2.1]-2-octenyl, H, Cl, H, 276-7°; H, 5-methylbicyclo[2.2.1]-2-hepten-6-yl, H, Cl, H, 197-9°. The compds. had stronger natriuretic activity than hydrochlorothiazid. Excretion of K was not increased to the same degree as that of Na.
 IT 859-24-5P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide
 RL: PREP (Preparation of)
 (preparation of)

RN 859-24-5 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

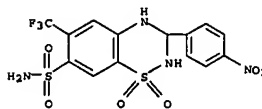
L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



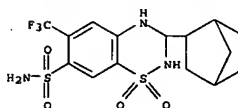
RN 748-19-6 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-chlorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 3872-12-6 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(p-nitrophenyl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

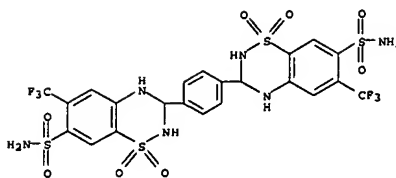


L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:7959 CAPLUS
 DOCUMENT NUMBER: 56:7959
 ORIGINAL REFERENCE NO.: 56:1537b-f
 TITLE: Dihydrobenzothiadiazine. Diuretic activity of some new derivatives
 AUTHOR(S): Sellari, Renato; Caldini, Oreste
 CORPORATE SOURCE: Lab. Manetti & Roberts, Florence
 SOURCE: Bollettino Chimico Farmaceutico (1961), 100, 323-9
 CODEN: BCFPAI; ISSN: 0006-6648
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 AB Cyclic deriva. of 4-amino-6-trifluoromethyl-m-benzenedisulfonamide (I) were synthesized by condensation with terephthalaldehyde (II), glyoxylic acid (III), phthalaldehydic acid (IV), pyruvaldehyde (V), phenylglyoxal (VI), and 4-biphenylglyoxal (VII). I (6.4 g.) and 1.34 g. II in 30 cc. 1,2-dimethoxyethane with one drop concentrated H₂SO₄ were refluxed 2 hrs. and poured into 150 cc. H₂O to give, after 24 hrs., p-bis(6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazin-3-yl)benzene, m. 300°. I (8 g.) and 8 g. III in 20 cc. H₂O with 1 drop H₂SO₄ were refluxed 0.5 hr., cooled, and dissolved in aqueous NaHCO₃ to give on acidification with dilute HCl 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazine-3-carboxylic acid (VIII), m. 238°. I (8 g.) and 3.75 g. IV in 50 cc. 1,2-dimethoxyethane with 1 drop H₂SO₄ were refluxed 2.5 hrs. and poured into 300 cc. H₂O to yield 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazine-3,3',7',7'- or (3,4',1',7')benzopyrrolidinone, m. 323° (H₂O). I (11 g.) and 11 g. V in 60 cc. H₂O were refluxed for 1 hr. while adding 60 cc. 95% EtOH, then heated 1.5 hrs. and filtered. The residue was washed with EtOH and dried to give 3-acetyl-6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 285-7° (EtOH). Similarly, 16 g. I and 7.38 g. VI, refluxed 2 hrs., gave the 3-benzoyl derivative, m. 240-2°, and 16 g. I and 11.6 g. VII gave the 3-(p-phenylbenzoyl) derivative, m. 241°. VIII (0.75 g.) in 5 cc. EtOH, treated with 0.558 N-diethylaminoethylthiocarbonyl bromine in 5 cc. EtOH, gave the salt, m. 178° (decomposition). Similarly, the VIII-N-diethylaminoethylthiocarbonyl, m. 195-8°, VIII-piperazine, m. 215-17°, and VIII-hexamethylenetetramine, m. 187°, salts were obtained. The compds. are useful as diuretics having an action equal to or stronger than dihydroflumethiazide.
 IT 1764-14-3P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide
 RL: PREP (Preparation)
 (preparation of)
 RN 1764-14-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

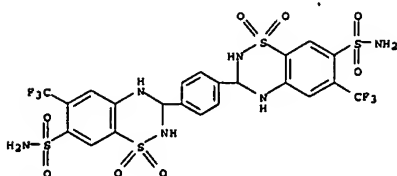


L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1962:7744 CAPLUS
 DOCUMENT NUMBER: 56:7744
 ORIGINAL REFERENCE NO.: 56:1466h-4,1467a
 TITLE: Bisbenzothiadiazine deriva
 INVENTOR(S): Bernstein, Jack; Yale, Harry Louis
 PATENT ASSIGNEE(S): Olin Mathieson Chemical Corp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3004024		19611010	US 1959-805374	19590410
PRIORITY APPLN. INFO.:			US	19590410

AB 3,3'-Bis(1,2,4-benzothiadiazine) 1,1-dioxide compds. (I), useful as diuretics and antihypertensives, containing particularly CF₃ and sulfamoyl or N-substituted sulfamoyl groups in the benzenoid rings were prepared by condensation of a dicarbonyl, acetal, or ketal compound or a bis(dihalomethyl) derivative with a substituted o-aminobenzenesulfonamide.
 Thus, 31.9 g. 5-amino-α,α,α-trifluoro-2,4-toluenedisulfonamide was refluxed 4 hrs. with 4.3 g. succinaldehyde in 250 ml. 95% EtOH and 25 ml. 10% aqueous HCl, the EtOH distilled, and the residue, after slowly distilling on a steam-bath with 25 ml. 20% aqueous HCl and 100 ml. EtOH, filtered to give 20 g. of an ether-washed solid. Two recrystns. from 90% aqueous MeCN gave 3,3'-ethylenebis(2,4-dihydro-6-trifluoromethyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide), m. 257-9° (decomposition).
 IT 1764-14-3P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide
 RL: PREP (Preparation)
 (preparation of)
 RN 1764-14-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN
 ACCESSION NUMBER: 1961:144261 CAPLUS
 DOCUMENT NUMBER: 55:144261
 ORIGINAL REFERENCE NO.: 55:27358f-1, 27359a-1, 27360a-b
 TITLE: Diuretics. V. 3, 4-Dihydro-1,2,4-benzothiadiazine 1,1-dioxides
 AUTHOR(S): Whitehead, Calvert W.; Traverso, John J.; Sullivan, Hugh R.; Marshall, Frederick J.
 CORPORATE SOURCE: Lilly Research Labs., Indianapolis, IN
 SOURCE: Journal of Organic Chemistry (1961), 26, 2814-18
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 55:144261

AB The synthesis and properties of 30 new 3-cycloalkenyl and 3-cycloalkyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were described. Correlations between their structures and biol. activity confirmed previously proposed analogies among similarly 3-substituted 1,4-unatad, and 1,4-dihydro derivs. of the benzothiadiazine 1,1-dioxide nucleus. The following 1-cycloalkenylacetoneitriles were prepared by a known method: 1-cycloheptenylacetoneitrile, 81% yield, b.p. 104°, n_{25D} 1.4808; 1-cyclopentenylacetoneitrile, 64%, b.p. 72-3°, n_{25D} 1.4672; 3-methyl-1(or 5)-cyclopentenylacetoneitrile, 80%, b.p. 78°, n_{25D} 1.4488; 2-methyl-1(or 5)-cyclopentenylacetoneitrile, 79%, b.p. 83-4°, n_{25D} 1.4672. 1-Cycloalkenylacetoneitrile (0.8 mole) in 200 ml. alc. was hydrogenated at room temperature over 2 g. 5% Pd-C with H at 50 lb./sq. in. and the cycloalkyl acetoneitrile distilled. 3-Methylcyclopentenylacetoneitrile (97% yield) b.p. 79°, n_{25D} 1.4411, and cycloheptylacetoneitrile (88%) b.p. 102°, n_{25D} 1.4654. A solution of 0.8 mole cycloalkylacetoneitrile or cycloalkenylacetoneitrile in 200 ml. dioxane and 400 ml. concentrated HCl refluxed 24-48 hrs., dioxane distilled in vacuo, the organic layer extracted with Et₂O, and then 2% NaOH, and the basic layer acidified gave the carboxylic acid, which was distilled to yield lactones of the 1-cycloalkenylacetic acids. Cycloheptylacetic acid (57% yield) b.p. 146-7°, and 1-cyclohexenylacetic acid (66% yield) b.p. 150-5°, n_{25D} 1.4852. 1-Cyclohexenylacetic acid and 2-oxohexahydrocyclopenta(b)furan (I) (approx. 1:1 mixture) (II), obtained in 41% yield, n_{25D} 1.4771, (64 g.) treated with SOCl₂ gave 25.6 g. 1-cyclohexenylacetyl chloride, b.p. 88-100°. I was obtained in 55% yield, b.p. 118-20°. 3-Methylcyclopentenylacetic acid (58%) b.p. 120-4°, n_{25D} 1.4472. 2-Oxooctahydrocyclohepta(b)furan (70%) b.p. 146-50° and 2-oxo-4(or 6a)-methylhexahydrocyclopenta(b)furan (74%) b.p. 111-12°, n_{25D} 1.4636. Mg (17.2 g.), 80 ml. Et₂O, 10 g. 4-norbornenylmethyl bromide, and a crystal of iodine treated (after the reaction started) with 121.8 g. more 5-norbornenylmethyl bromide in 250 ml., Et₂O added, and the mixture refluxed 1 hr., poured into dry ice in Et₂O, acidified, and extracted gave 65.5 g. 5-norbornenylacetic acid, b.p. 129°, n_{25D} 1.4878. Cycloalkyl- and cycloalkenylacetic acids were converted to the acid chlorides with SOCl₂. The amides were prepared in the usual manner; the

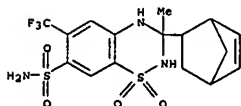
L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
 acid chlorides were treated with PhNHMe or NMe₂ and CSH₅N in C₆H₆, the solns. washed with H₂O, dried, and evapd. and the amides yielded in vacuo. The following RCH₂CONMe₂ were thus obtained (R, R', 1, yield, b.p./mm. given): 2-cyclopentenyl, Me, 79, 85°/0.25; 1-cyclohexenyl, Me, 75, 95°/0.4; cyclopentyl, Ph, 80, 130°/1; 1-cyclohexenyl, Ph, 80, 130°/0.3; 2-cyclohexenyl, Ph, 82, 130°/0.3; 3-cyclohexenyl, Ph, 90, 132°/0.3; cyclohexyl, Ph, 95, 136°/0.4; 3-methylcyclopentyl, Ph, 88, 104°/0.08; 5-norbornenyl, Ph, 95, 117°/0.08; cycloheptyl, Ph, 95, 154°/1; 1-methylcyclohexyl, Ph, 98, 151°/4.5. N-Methylcycloalkyl- or N-methylcycloalkenylacetanilides (1 mole) in 220 ml. tetrahydrofuran treated in 2 hrs. with 6.25 g. LiAlH₄ suspended in 150-200 ml. tetrahydrofuran, the mixt. stirred overnight and treated with dil. alc., and the product distr. gave the aldehydes. The following compds. were obtained: 2-cyclopentenylacetaldehyde, 46.5%, b.p. 53-6°, n_{25D} 1.4604; cyclopentenylacetaldehyde, 55%, b.p. 53°, b. 156°; cyclohexenylacetaldehyde, 45%, b.p. 68-70°, n_{25D} 1.4615; 2-cyclohexenylacetaldehyde, 33%, b.p. 65°; 3-cyclohexenylacetaldehyde, 27%, b.p. 87-127°; 3-methylcyclopentenylacetaldehyde, 44%, b.p. 63-6°, n_{25D} 1.4421; 1-methylcyclohexenylacetaldehyde, 39%, b.p. 82-5°, n_{25D} 1.4619; cycloheptylacetaldehyde, 33%, b.p. 98-103°, n_{25D} 1.4652; 5-norbornenylacetaldehyde, 32%, b.p. 76-8°, n_{25D} 1.4851. The following RCH₂CH₂NNHCONH₂ were obtained (R and m.p. given): 2-cyclopentenyl, 116-17°; 3-cyclohexenyl, 142-4°; 3-methylcyclopentyl, 126-7°; cycloheptyl, 160-1°; 1-methylcyclohexyl, 170-1°. The following 2,4-(NO₂)₂C₆H₃NNH:CHNCH₂R were obtained (R and m.p. given): 2-cyclopentenyl, 98-9°; cyclopentyl, 128-9°; 2-cyclohexenyl, 97°; 3-methylcyclopentyl, 91-2°; 5-norbornenyl, 124-5°; cycloheptyl, 96-7°. Li diethoxyaluminum hydride (0.156 mole) in Et₂O was added in 0.5 hr. to 0.26 mole of the N,N-dimethylcycloalkenylacetamide in 200 ml. Et₂O at 0-5°, the mixt. stirred 12 hrs. at room temp. and hydrolyzed with 2N H₂SO₄ at 0°, and the aldehyde-Et₂O soln. washed, dried, and distd. in vacuo. 2-Cyclopentenylacetaldehyde was obtained in 23% yield, b.p. 53°, and 1-cyclohexenylacetaldehyde in 17% yield, b.p. 53-54°. 4-Amino-6-chlorobenzene-1,3-disulfonamide (28.5 g.) in 400 ml. 50% 6N HCl and alc.; 31.9 g. 4-amino-6-trifluoromethylbenzene-1,3-disulfonamide in 200 ml. 50% 6N HCl and alc.; and 33 g. 4-amino-6-bromobenzene-1,3-disulfonamide in 300 ml. warm 50% 6N HCl and alc. suspensions were prepd. The appropriate aldehyde was added to each suspension and the mixt. shaken 0.5 hr., cooled after standing 12 hrs. at room temp., the product washed, and the resultant 3,4-dihydro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were dissolved in warm alc. and distd. with H₂O. The product was recrystd. from dil. alc. The following 3,4-dihydro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were obtained (3 and 6 substituents, 1 yield, and m.p. given): 2-cyclopentenylmethyl, Cl, 71, 222°; cyclopentylmethyl, Cl, 84, 230°; cyclopentylmethyl, Br, 80, 228°; hexylmethyl, Cl, 40, 172°; 2-cyclopentenylmethyl, CF₃, 70, 148°; 2-cyclohexenylmethyl, Cl, 85, 221°; 2-cyclohexenylmethyl, Br, 80, 215°; 3-cyclohexenylmethyl, Cl, 35, 215°; 3-cyclohexenylmethyl, Br, 32, 202°; cyclopentylmethyl, CF₃, 70,

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 156°; 1-cyclohexenylmethyl, Cl, 65, 225°; 3-methylcyclopentylmethyl, Cl, 80, 198°; 3-methylcyclopentylmethyl, Br, 80, 100°; cyclohexylmethyl, Cl, 85, 232°; cyclohexylmethyl, Br, 80, 214°; 5-norbornenyl, Cl, 40, 210°; 2-cyclohexenylmethyl, CF₃, 86, 202°; 3-methylcyclopentylmethyl, CF₃, 85, 185°; cycloheptylmethyl, Cl, 93, 215°; cycloheptylmethyl, Br, 76, 214°; 1-methylcyclohexylmethyl, Cl, 35, 245°; 5-norbornenylmethyl, CF₃, 76, 228°; cycloheptylmethyl, CF₃, 60, 178°; 1-methylcyclohexylmethyl, CF₃, 32, 190°; 2,3-dihydro-2-(γ-pyranyl), Cl, 30, 235°; 5-norbornenyl, Cl, 46, 234°; 2-norbornyl, Cl, 80, 263°; 6-methylcyclohexenyl, Cl, 75, 230°; 6-methylcyclohexenyl, Br, 78, 230°; 6-methyl-5-norbornenyl, Cl, 40, 235°. 6-Chloro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (0.1 mole) in 75 ml. tetrahydrofuran was treated with 1.5 g. NaBH₄, treated dropwise with 1.5 g. AlCl₃ in 50 ml. tetrahydrofuran, the mixt. refluxed 2 hrs., kept overnight, and decompd., and the solids sepd. and crystd. The following results were obtained (compd., 1 yield, and m.p. given): 6-chloro-3-cyclopentylmethyl-3,4-dihydro-7-(N-methylsulfamoyl)-1,2,4-benzothiadiazine 1,1-dioxide, 12, 174-5°; 6-chloro-3-cyclohexenylmethyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, 60, -; 6-chloro-3-cyclopentylmethyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, 40, -. The saluretic and diuretic activities of the compds. listed above were greater than those of the parent compd.

IT 1581-31-3P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-ylmethyl)-6-(trifluoromethyl)-, 1,1-dioxide RL: PREP (Preparation)

RN 1581-31-3 CAPLUS

CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-ylmethyl)-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)



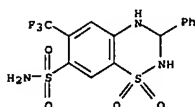
L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2007 ACS ON STN
 ACCESSION NUMBER: 1961:105988 CAPLUS
 DOCUMENT NUMBER: 55:105988
 ORIGINAL REFERENCE NO.: 55:19971b-g
 TITLE: Benzothiadiazine derivatives
 INVENTOR(S): Lund, Frantz; Godfredsen, Wagn O.
 PATENT ASSIGNEE(S): Lovens Kemiske Fabrik ved. A. Kongsted
 DOCUMENT TYPE: Patent
 LANGUAGE: Unavailable
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 863474		19610322	GB	
DE 1226107			DE	
DK 97587			DK	
US 3254076		1966	US	
US 3254077		1966	US	

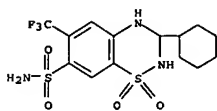
AB 6-Substituted 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I), prepared from a substituted 2,4-disulfamoylaniline (II) and RCHO, H₂C(OMe)₂, or H₂C(CHOR), had saluretic effects in rats and humans. Thus, a solution of 3.2 g. 5-trifluoromethyl-2,4-disulfamoylaniline, 25 ml. EtOH, and 10 ml. ethylal, and a catalytic amount of p-MeC₆H₄SO₃H was refluxed overnight and worked up to give the 6-trifluoromethyl derivative of I, m. 271-2°. By varying RCHO (or acetal) reactant, the following 3-substituted-6-trifluoromethyl analogs of I were prepared: Me (from EtOCH₂CH₂Cl, EtOCH₂ClMe, or ClCH₂CHO), m. 240-40.5°; ClCH₂, m. 245-45.5°; BrCH₂ (III), m. 209-10°; Et, m. 255-6°; Pr, 232-3°; iso-Pr, m. 244-5°; Bu, m. 216-17°; 5-hydroxybutyl, m. 175-5.5°; n-pentyl, m. 190-1°; γ-nitropentyl, m. 243-5.5°; acetonyl, m. 208-9°; β-methoxyethyl, m. 188-90°; dicarbethoxymethyl, m. 232-4°; Ph, m. 218-19.5°; Ph₂CH, m. 261-2.5°; p-methoxyphenethyl, m. 250-1.5°; benzyl (IV), m. 224-5°; phenethyl, m. 235-6°; α-phenylethyl (V), m. 243-4°; p-chlorobenzyl, 243-4°; benzoyloxymethyl, m. 221-21.5°; phenoxyethyl, m. 244-6°; p-nitrophenoxyethyl, m. 261-2° (decomposition); p-aminophenoxyethyl, m. 193-4°; 2,4-dichlorophenoxyethyl, m. 230-1°; Bz, 261-2°; benzylthiomethyl, 202-3°; β-benzylthioethyl, 134-46°; 2-pyridyl, m. 304-6° (decomposition); 2-furyl, m. 190-2°; 1-cyclohexyl, m. 258-9°; 1-propenyl, m. 213-5°; n-hexyl, 178-9°; 3-pyridyl, m. 240-1°; ateryl, m. 167-9°.

Substitution of a ketone for the aldehyde reactant yields the corresponding 3,3-disubstituted-6-trifluoromethyl analog of I; thus, acetone and 6-trifluoromethyl derivative of II gave the 3,3-dimethyl-6-trifluoromethyl derivative of I. The following were prepared similarly: 3-methyl-3-ethyl, m. 212-13°; 3-methyl-3-chloro (VI), m. 227-7.5°; 3-methyl-3-carbethoxy, m. 191-4°; 3-methyl-3-carbomethoxy, m. 150-2°; cyclopentane-1,3-epi, m. 232-4°; cyclohexane-1,3-epi, m. 261-2°; 2-chlorocyclohexane-1,3-epi, m. 218-19°; 4-chlorocyclohexane-1,3-epi (VII), m. 217-18°. By varying the 5-substituent in II, the following 3,3-dimethyl-6-substituted-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides were prepared: NO₂, m. 233-3.5°; Cl (VIII), m. 230-1°; Br, m. 228-9°; MeO, m. 240-0.5°;

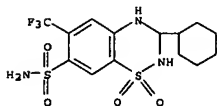
L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
 Me, m. 243-4°; H, m. 242-2.5°. The following were prep.
 similarly (substituents given): 3-Me, 3-Et, 6-Cl, m. 231-3°; 3-Me,
 3-ClCH₂, 6-NO₂; 3-Me, 3-CO₂Me, 6-NO₂, m. 218-19°;
 cyclopentane-1,3-spiro-6-chloro, m. 234°; cyclohexane-1,3-spiro-6-
 bromo (IX), m. 281-3°; 2-methylcyclohexane-1,3-spiro-6-bromo, m.
 231-3°; 2-chlorocyclohexane-1,3-spiro-6-chloro, m. 223-5°;
 3-methyl-3-acetyl-6-chloro, m. 246-7°. Tests on groups of ten
 persons indicated that 2.0 mg. IV had the same saluretic effect as 20 mg.
 of the 6-Cl deriv. of I. III-IX were potent saluretic agents in rates.
 IT 1170-25-8P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 4454-81-3P
 (trifluoromethyl)-, 1,1-dioxide
 RL: PREP (Preparation)
 (preparation of)
 RN 1170-25-8 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-
 (trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



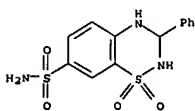
RN 4454-81-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-
 (trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)



L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 100395-18-4 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-
 1,1-dioxide (6CI) (CA INDEX NAME)



L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1961:39254 CAPLUS
 DOCUMENT NUMBER: 55:39254
 ORIGINAL REFERENCE NO.: 55:7664d-f
 TITLE: Aromatic sulfamoyl compounds with diuretic action
 AUTHOR(S): Lund, P. J.; Kobinger, W.
 CORPORATE SOURCE: Research Labs. Leo Pharm. Prods., Copenhagen
 SOURCE: Acta Pharmacologica et Toxicologica (1960), 16,
 297-324
 CODEN: APTQ66; ISSN: 0001-6683

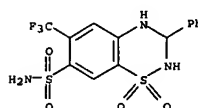
DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A relation was found between constitution and activity of substituted
 2,4-disulfamoylanilines (DSA) and substituted 7-sulfamoyl-3,4-dihydro-
 1,2,4-benzothiadiazine 1,1-dioxides (DBT). DSA and DBT compds. showed a
 distinct relation between substitution in the benzene ring and saluretic
 activity. Substitution in the heterocyclic ring of DBT compds. yielded
 some substances considerably more potent than the known
 hydroflumethiazide
 (6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine
 1,1-dioxide) and hydrochlorothiazide. Of these substances,
 benzylhydroflumethiazide (Cetyl) (the 3-benzyl derivative of
 hydroflumethiazide), which in human expts. showed the saluretic activity
 expected on the basis of the animal expts., was selected for further
 clin.

use. Among the active substances studied, no differences in the urinary
 electrolyte-excretion pattern were detected by the method used.

IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 4454-81-3
 , 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-
 (trifluoromethyl)-, 1,1-dioxide 100395-18-4,
 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-
 1,1-dioxide
 (as diuretic)

RN 1170-25-8 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-
 (trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 4454-81-3 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-
 (trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)

L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1960:11460 CAPLUS
 DOCUMENT NUMBER: 54:11460
 ORIGINAL REFERENCE NO.: 54:2351f-1,2352a-f
 TITLE: Synthesis of trifluoromethylated compounds possessing
 diuretic activity
 AUTHOR(S): Holdrege, Charles T.; Babel, Richard B.; Cheney, Lee
 C.
 CORPORATE SOURCE: Bristol Labs., Inc., Syracuse, NY
 SOURCE: Journal of the American Chemical Society (1959), 81,
 4807-10
 CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 54:11460

AB Hydrated Na₂S (113.5 g.) (containing 61% Na₂S), 28.4 g. S, and 500 cc.
 H₂O

warmed on the steam bath to solution, the solution added dropwise with
 stirring
 to 400 g. 4,3-Cl(O₂N)C₆H₃CP₃ in 1.5 l. refluxing MeOH, refluxed 1 hr.,
 cooled, and filtered yielded 359 g. [4,2-CP₃(O₂N)C₆H₃S]₂ (II), m.
 158-61° (AcOH). I (1000 g.) in 2.3 l. glacial AcOH and 250 cc. H₂O
 treated 4 hrs. at 5-14° with gaseous Cl₂, heated 2 hrs. at
 70°, cooled to 10°, chlorinated again 7 hrs., kept
 overnight, heated 0.5 hr. on the steam bath, and poured into 6 l. ice and
 H₂O, the aqueous phase extracted with 1 l. PhMe, and the combined
 organic phase and

extract evaporated gave crude 4,2-CP₃(O₂N)C₆H₃SO₂Cl (III). The crude II

added
 during 3 hrs. to 2 l. cold concentrated NH₄OH below 15°, kept overnight,
 and filtered, the residue slurried with 4 l. 10% aqueous NaOH at 15°,
 filtered, acidified below 25°, cooled, and filtered, and the
 residue recrystd. from 2 l. iso-PrOH gave 490 g. 4,2-CP₃(O₂N)C₆H₃SO₂NH₂
 (III), m. 165-7°; 2nd crop 66 g. A similar run with double the
 chlorination time yielded 54% III. III (5 g.) and 5 cc. glacial AcOH in
 150 cc. H₂O heated on the steam bath while being treated with 6 g. Fe
 filings in 2 portions 5 min. apart, stirred 3 hrs. on the steam bath,
 diluted with 100 cc. 95% EtOH, heated to boiling, filtered, neutralized

hot
 with saturated aqueous Na₂CO₃, filtered, and cooled gave 3 g. 2-NH₂

analog (IV) of
 III, m. 143-6° (aqueous EtOH). Fe filings (242 g.) added in portions
 during 1.5 hrs. to 242 g. NH₄Cl, 190 g. III, 2 l. MeOH, and 1 l. H₂O, the
 mixture refluxed 1.5 hrs., and filtered hot, the cake washed with 400 cc.
 MeOH, the combined filtrates diluted with 4.5 l. H₂O, heated to boiling,
 filtered, and cooled to 0°, and the precipitate recrystd. from a mixture

of
 400 cc. H₂O and 250 cc. MeOH containing 2 cc. 6N HCl yielded 126 g. IV,
 m.

141-5°. IV (35 g.) added during 0.5 hr. to 96 cc. ClSO₃H with
 stirring and cooling, the mixture treated without cooling during 1 hr.

with
 87.6 g. NaCl, heated rapidly in a bath from 85 to 150°, kept 15
 min. at 150°, and poured into 600 g. ice and H₂O precipitated gummy
 4,6,1,3-H₂N(F₃C)C₆H₂(SO₂Cl)₂ (V). The crude V added to 200 cc.
 concentrated

NH₄OH, kept overnight, heated on the steam bath, and cooled gave 15.7 g.
 4,6,1,3-H₂N(F₃C)C₆H₂(SO₂NH₂)₂ (VI), m. 239.5-41.5° (H₂O). VI (1
 g.) and 4 cc. 98% HCO₂H refluxed 4 hrs., cooled, and filtered gave
 7-sulfamoyl-6-trifluoromethyl-2H-1,2,4-benzothiadiazine 1,1-dioxide

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 m. 100-2° (cor.) (1:1 95% EtOH-H₂O). IV (45 g.) chlorosulfonated in the usual manner, 1/2 of the resulting V extd. with 125 cc. dioxane, the ext. treated with 15 cc. 40% aq. CH₂O, kept at 10° overnight, basified with 125 cc. concd. NH₄OH, kept 1.5 hrs. at room temp., heated 1 hr. on the steam bath, refluxed 2.5 hrs., cooled with ice, and filtered yielded 0.6 g. 3,4-dihydro deriv. (VIII) of VII, m. 260-4° (aq. EtOH). VI (63.8 g.), 16.5 g. 40% aq. CH₂O, 300 cc. H₂O, and 0.1 cc. concd. H₂SO₄ refluxed 3.5 hrs. with stirring, cooled, and filtered, and the residue recrystd. with 1.5 g. C from 400 cc. MeOH and 200 cc. H₂O gave 43.5 g. VIII, m. 262-5°, 271-4° (cor.). Crude V from 22 g. IV added to 250 cc. 40% aq. MeNH₂, kept overnight at room temp., and filtered, the filtrate concd., cooled, and filtered, and the residue dissolved in the min. amt. of MeOH at room temp. and repptd. with an equal vol. of H₂O gave 11 g. 4,6,1,3-H₂N(P₃C)C₆H₂(SO₂NHMe)₂, m. 168-70° (H₂O). VI (5 g.) and 45 cc. Me₂C(OMe)₂ refluxed 24 hrs. and evapd. gave 1.6 g. 3,3-di-Me deriv. of VII, m. 216-21° (aq. MeOH). VI (5 g.), 0.0173 mole appropriate aldehyde, 1 drop concd. H₂SO₄, and 30 cc. H₂O refluxed, cooled, and filtered, and the residue recrystd. from Et₂O aq. MeOH or aq. Me₂CO gave the corresponding 3-substituted VII (IX); method A. VI (5 g.), 0.0173 mole appropriate aldehyde, and 30 cc. glacial AcOH refluxed and evapd. in vacuo, and the residue recrystd. from aq. MeOH gave the corresponding IX; method B. VI (5 g.), 0.0173 mole ethylene ketal of an appropriate cycloalkanone, 2 drops concd. H₂SO₄, and 50 cc. BuOH refluxed and evapd. in vacuo, and the residue recrystd. from aq. MeOH yielded the corresponding IX; method C. By these methods were prepd. the following IX (3-substituent, m.p., method, reactant, % yield, and reflux time given): Et, 262-3° (decompn.), A, EtCHO, 59, 4; Me, 247-50° (decompn.), A, AcH, 70, 0.25; PhCH₂, 221-3°, B, PhCH₂CHO, 35, 16; 2-pyridyl, 310-11°, A (without the H₂SO₄ catalyst), 2-CSH₄CHO, 19, 0.5; CCl₃, 283-5° (decompn.), A, CCl₃CH(OH)₂, 22, 24; Ph, 220-4°, B, BzH, 17, 24; pentamethylene, 260-2°, C, cyclohexanone ethylene ketal, 23, 1.5; tetramethylene, 225-6° (decompn.), C, cyclopentanone ethylene ketal, 19, 2. VI and VII were potent orally active diuretics of low toxicity; VII was about 10 times as active orally as VI in animals.
 IT 1170-25-8P, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
 RL: PREP (Preparation)
 (preparation of)
 RN 1170-25-8 CAPLUS
 CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)

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